RECURRENT PERICARDIAL EFFUSION OF UNKNOWN ETIOLOGY

REPORT OF A CASE WITH STUDIES OF THE CIRCULATION AND OF ABSORPTION FROM THE PERICARDIAL CAVITY*†

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There has been under our observation for 21 months a patient who has presented an unusual lesion involving the pericardium, namely recurrent chronic pericardial effusion, for the occasion of which we have so far been unable to ascertain or establish the mechanism. We have been unable to find in the literature a situation similar to it and on this account it appeared to be of interest to describe the case. Moreover, the opportunity was afforded us of making certain studies of the circulation.

The function which the pericardium serves has not been clearly defined. The notion is current that its chief function is to prevent rapid dilatation of the heart[1]. Too much emphasis may have been placed on this point. Congenital absence of the pericardium occurs in man and individuals exhibiting this defect have not appeared to have suffered circulatory embarrassment[2,3]. Moreover, in dogs the pericardium may be excised without giving rise to untoward effects[4]. The pericardium is a none too distensible sac when subjected to acute stretching, but is capable of rather remarkable distensibility when it is put to the test gradually. The lesions to which it is subject give it unusual significance even though its exact function has not yet been defined. The pericardium is subject on the one hand to lesions which give rise to the accumulation of fluid in the pericardial cavity, and on the other hand to lesions leading

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to the formation of adhesions, which may be external or internal or both. In fact, the first, fluid, may be the forerunner of the second, adhesions. In both situations the function of the enmeshed organ, the heart, may be interfered with seriously. With regard to the former lesion—pericardial effusion—there is point in knowing to what extent it interferes with the circulation, because of the frequency of its occurrence in the course of rheumatic infection, tuberculosis, empyema, as a consequence of other infections involving its surface, uremia, and occasionally congestive heart failure. It may be of sufficient quantity to give rise to cardiac tamponade. Cohnheim[5] described clearly the consequences of acute distention of the pericardium in animals. As a matter of fact, up to the present the information which is available has been derived for the most part from observations made of animals. Patients exhibiting pericardial effusion are too sick in most instances to cooperate in prolonged and detailed observations. Furthermore, neither the mechanism of the formation of pericardial fluid, nor of its absorption, nor the factors controlling its quantity under normal circumstances are precisely known. In short, there is a provocative lack of knowledge pertaining to the pericardium. We have had opportunity in the case of this patient to make certain observations leading to a clearer insight into these mechanisms.

In this paper is recorded a description of this unusual case exhibiting chronic pericardial effusion, together with certain quantitative measurements of the circulation in the presence of cardiac tamponade, as well as certain observations relating to absorption of dyes from the pericardial cavity. A more detailed study of the measurements of the circulation will be made elsewhere.

All observations were made with the patient in a basal metabolic state: rebreathings for the calculation of the arteriovenous oxygen difference, the oxygen consumption, the vital capacity, the circulation time, the venous pressure, the height and weight, the electrocardiogram, the x-ray photograph of the heart, the blood pressure. Measurements

of cardiac output were made by the Grollman method, the three sample technique being employed[6]. The estimation of the arm to tongue circulation time was made by the use of decholin[7]. The venous pressure was measured by the direct method[8].

E. C., History No. 94114, a white female, 14 years of age, was admitted first to the New York Hospital on April 12, 1935, complaining of swelling of the eyelids, cyanosis, dyspnea on exertion, and frequency of urination of six years duration. There was no family history of tuberculosis. The past history contained no significant facts.

The present illness began in 1928, when the patient was seven and a half years of age. At this time swelling of the eyelids and lips appeared. At the end of six weeks, during which the patient experienced headache, she was admitted to the New York Nursery and Child's Hospital on October 29, 1928. An abstract of the data at this time discloses these facts: There was edema of the face, bilateral hydrothorax, ascites, and enlargement of the liver to the level of the umbilicus. The systolic blood pressure measured 100 mm. of mercury, the diastolic 75 mm. There were no murmurs of the heart. The examination of the urine revealed no abnormalities. The Wassermann reaction of the blood was negative. Tuberculin reaction of the skin was negative. The serum proteins amounted to 7.3 gm. per cent. The fluid removed from the pleural cavity appeared to be a transudate. The electrocardiogram showed complexes of low amplitude with a slight tendency to right axis deviation. X-ray photograph of the chest confirmed the diagnosis of bilateral pleural effusion and suggested the "presence of pericarditis." As a consequence of the removal of the pleural fluid by paracentesis and the use of diuretics, the patient improved and was discharged from the hospital.

She was readmitted to the same hospital in February, 1931 because of recurrence of symptoms. Again, after treatment by measures similar to those used before, she improved sufficiently to be discharged. After that time she was seen at irregular intervals. In 1933 the patient observed cyanosis of the hands and feet. Because of the

reappearance of ascites, admission to New York Hospital was recommended, and she was admitted suffering from the complaints already recorded.

Examination at this time revealed an under nourished, under developed girl, who looked younger than her stated age of 14 years. As a matter of fact she was approximately the size of the average child of 8 years. Her mental development had not been retarded. The combination of these two factors—undersize and normal mental capacity—gave the child a semblance of precocity. There was cyanosis of the lips and nail beds. The face was puffy. The retinal vessels were engorged. The heart rate was rapid, the pulse of small volume. The superficial veins were distended, especially those of the neck. In fact, the venous pressure measured 135 mm. of saline (normal usually less than 100 mm. by this method). The systolic blood pressure measured 120 mm. of mercury, the diastolic 80 mm. There were signs of a moderate amount of fluid in the left pleural cavity. The percussion of the heart showed it enlarged both to the right and to the left. There were no murmurs of the heart. The heart sounds were moderately loud. The fluoroscopic examination of the heart revealed a large cardiac silhouette having almost no visible pulsation. The configuration of the shadow was compatible with the diagnosis of pericardial effusion. There were signs of fluid in the peritoneal cavity. After removal of 1900 c.c. of greenish yellow ascitic fluid (April 13, 1935) the liver was found to be enlarged. Tap of the pericardium having been decided upon, 1100 c.c. of yellowish green fluid was removed. After its removal the cardiac shadow in the x-ray photograph was smaller, but remained large, still. The hilal markings were increased, and the lung markings were accentuated. The patient's condition improved following the pericardial tap. It may be stated at this time that guinea pigs inoculated with pericardial fluid on two occasions and ascitic fluid on one occasion did not develop tuberculous lesions. Tuberculin skin test at this time as well as on another occasion was negative. She was given ammonium chloride and

salyrgan and theocalcin with moderate diuretic effect. Having lost 3 kgm. in weight, she was discharged on May 6, 1935. During this admission the count of the red blood cells was 4,700,000, of the white blood cells 11,600. The hemoglobin amounted to 95 per cent (Sahli) on a basis of 14.5 grams being equivalent to 100 per cent. The serum proteins amounted to 6.0 grams per cent. The examination of the urine was essentially negative. In the concentration test the specific gravity of the urine rose to 1.027. She excreted 45 per cent of the phenolsulphonephthalein in 45 minutes, and 75 per cent of it in two hours. The electrocardiogram showed complexes of low voltage (Fig. 3).

It was suspected at this time that the patient's symptoms and signs were due to an accumulation of fluid in the pericardial cavity, in short, that pleural effusion, ascites, enlargement of the liver, edema of the face, distention of the neck veins, elevation of venous pressure, occurred as a consequence of cardiac tamponade, a notion that was confirmed later. The etiology of the pericardial lesion was, however, not known.

The patient was readmitted May 23, 1935 because of recurrence of cyanosis, edema of face and now of legs, orthopnea, ascites and pleural effusion. On this occasion 600 c.c. of fluid was removed from the pericardial cavity (2nd tap) on May 25, 1935. The patient was relieved of her symptoms by this measure and the signs of the other accumulations of fluid (pleural and abdominal) decreased. Giving salyrgan resulted in diuresis of 1930 c.c. at a time when the fluid intake was 1050 c.c. There was gradual recurrence of pericardial fluid with the signs and symptoms of tamponade again appearing. Experience showed that pericardial tap was required at approximately four week intervals, and was followed on each occasion by relief of the symptoms. From the time of the first tap, April 24, 1935 to November 5, 1935 (7 months) 7 taps were necessary. The amount removed varied between 500 c.c. and 1500 c.c., but it was in most instances greater than 1000 c.c.

During this time (7 months) we had the opportunity of making many observations of the circulation before and

after removal of fluid by pericardial tap (see observation and discussion). X-ray and fluoroscopic examinations after removal of fluid did not reveal calcification of the pericardium. It was found that the administration of theocalcin and salyrgan or mercupurin delayed the recurrence of secondary consequences of venous obstruction, ascites and pleural effusion. Observation on many occasions allow us to make these generalities: Following tap, the relief of the patient's symptoms was striking: dyspnea, cyanosis and distention of neck veins diminished at once; the next day the face was no longer swollen and ascites and pleural effusion decreased. Improvement continued for a week or ten days, when the patient then observed a gradual recurrence of symptoms, increasing in severity until pericardial tap was again necessary. It was apparent that the patient was suffering from a pericardial lesion giving rise to recurrent effusion. Since it did not appear to be tuberculous in its nature, and organic lesion of the heart could not be detected, and there was no evidence of rheumatic infection, the nature of the lesion was a matter of speculation only.

That there might be pericardial adhesions giving rise to multiple loculations, or to mechanical obstruction appeared to be a possibility. Because pericardial taps were required at shorter intervals an exploratory operation was decided upon at the time of the seventh admission in November, 1935. This decision having been made, pericardial tap was done. In an interval when the patient was at her best she was transferred to the Surgical Service and operated on by Dr. George J. Heuer on November 15, 1935, under ether and oxygen anesthesia.

Operation: Exposure of the pericardium was made by removal of the third and sixth costal cartilages. The pericardium was exposed over an area 6 cm. square. Outwardly it appeared normal. There were no external adhesions. The pericardium was incised and 800 c.c. of fluid removed slowly. The patient suffered no untoward effects as a consequence of release of the intrapericardial pressure. The sac was then opened more widely. The heart was not

enlarged. There was a fibrous exudate covering it. There were no adhesions between the visceral and parietal pericardium and no bands which could have caused obstruction were detected. The heart was freely movable. There did not appear to be obstruction about the superior or the inferior vena cava. The parietal surface was smooth and glistening. Tubercles were not present. A strip of pericardium was removed for microscopic examination and in sewing up the layers, the pericardial edges were not approximated but the cavity was left open to the mediastinum. Following operation there was rise in temperature, 38.6° C. (mouth), but this fell to normal in six days. When accumulation of fluid in the left chest and pericardial cavity occurred rapidly the output of urine was increased by giving mercupurin every three days. She began sitting up on November 29, 1935. Removal of 1400 c.c. of pericardial fluid was required on December 5, 1935 (8th tap). She was discharged December 8, 1935, to be followed in the Cardiac Clinic. The ninth tap was required on December 17, 1935, and from that time until November 19, 1936, seventeen taps have been necessary. The total number of taps was twenty-three from the time of the first, April 27, 1935, to November 19, 1936. The amount of fluid has varied between 600 c.c. and 1800 c.c. On each occasion the pulse was paradoxical in type when fluid was present and lost this characteristic after its removal. During this time the patient's regime has been as follows: She takes a diet which has low salt and high protein content. The daily fluid intake is limited to 1200 c.c. Between pericardial taps the patient is given 1.0 to 2.0 c.c. mercupurin intravenously at 7 to 10 day intervals. The patient's general condition has remained unchanged. Menses have not yet started. The height has increased from 139.5 cm. (April, 1935) to 143.0 cm. (November, 1936) in 21 months. Her weight when she was free of fluid in April, 1935 was 27.8 kgm. and it was, in November, 1936, 29.0 kgm. at a comparable time in her state of well-being. There has been no rise in temperature. She attends school and obeys her own inclination as to activities which, as experience has shown, do

not alter the velocity of the reaccumulation of fluid. Taps were necessary every 3 to 4 weeks. Recently, however, the interval has appeared to be a few days longer. Moreover, ascites does not recur to the same extent as formerly. The implications of these two observations are not clear. Exploratory operation has not appeared to alter the course significantly.

During this time there has been no significant change in red blood cell count or in hemoglobin. The serum proteins have remained normal (6.6 gm. per cent, albumin 4.2 gm. per cent, globulin 2.2 gm. per cent on May 11, 1935) on each occasion they have been examined. On October 16, 1936 the low value of 5.5 gm. per cent (albumin 2.8 gm. per cent, globulin 2.2 gm. per cent) was obtained after tap when dilution of the blood may have been present as a consequence of diuresis[9].

The fluid removed from the pericardial cavity has exhibited on all occasions essentially the same characteristics. The specific gravity varied between 1.016 and 1.020, the cell count from 30 to 70 cells, most of them lymphocytes, per c. mm. The total protein content of the fluid measured 6.2 gm. per cent (albumin 2.5 gm. per cent, globulin 3.7 gm. per cent) on April 20, 1936. As has already been indicated, guinea pigs inoculated with fluid on April 25, 1935 and December 21, 1935, and with ascitic fluid on March 16, 1936, did not develop tuberculous lesions.

Procedure of Pericardial Tap

Before the first few taps were performed the patient was given morphine or amytal. It was found, however, that nausea and vomiting frequently occurred after the operation. The patient then requested that drugs be withheld; since this has been done she has experienced no discomfort.

The patient is propped up in bed, so that she is sitting almost upright. The operation is carried out under the usual sterile precautions. After infiltration of the skin and subcutaneous tissue with novocaine an 18 gauge needle is inserted in the fifth rib interspace, slightly outside the nipple line. The needle is inserted parallel to the chest

wall so that it enters the pericardial cavity parallel to the heart. Before inserting the needle it is attached to a 3-way stop-cock and a 50 c.c. syringe. On each occasion fluid has been readily obtained. It is drawn into the syringe and delivered by the stop-cock into a beaker. The use of a syringe permits slow removal of the fluid. During removal of the fluid respirations become easier, the neck veins less distended and cyanosis fades. The apical impulse may become visible and toward the end of the tap the cardiac impulse has been felt at times against the needle. When this occurred the patient did not complain of pain but experienced a vague uneasiness. As much fluid is removed at each tap as can be obtained.

Before discussion of the therapeutic measures which present themselves in the case of this patient, the salient features which serve to delineate the situation might be recapitulated. This patient, suffering from recurrent pericardial effusion, has been observed by us over a period of 21 months. As we have already described, she develops signs and symptoms of cardiac tamponade which have been found by experience to be a consequence of pericardial effusion. Removal of the pericardial fluid results in the disappearance of signs and symptoms for 10 to 14 days with a gradual return over the ensuing 10 to 14 days, when tap is again required. Over a period of 21 months, 23 therapeutic pericardial taps have been required. At first it was the notion that the patient was suffering from a tuberculous lesion of the pericardial cavity. Guinea pigs inoculated with the pericardial fluid and abdominal fluid, however, did not develop tuberculous lesions and on the other hand, the patient has a negative tuberculin test. Section of the pericardium later revealed chronic inflammatory tissue only. The lining layer of mesothelial cells was lacking. X-ray of the chest did not show evidence of tuberculous lesion of the parenchyma of the lung. The patient neither exhibited on examination nor gave a history of the stigmata of rheumatic infection. It seemed to us that exploratory investigation of the pericardial sac was in order; by chance there might be mechanical obstruction leading to the

accumulation of fluid in the sac. None was found at operation and the microscopic examination of the sac did not reveal evidence of acid fast infection. This operation, viewed after one year, has not appeared to alter the course of the disease.

THERAPY

Several methods of therapeutic approach to this problem other than those already tried have been considered but we have been unwilling to resort to any of them. These may be discussed briefly.

1. Simple opening of the pericardial sac and leaving it open to the mediastinum did not result in alteration of the course, since reaccumulation of fluid continues to occur. Either the two edges of the pericardium finally approximated and healed, or the margins of the sac adhered to the mediastinum, and the anterior mediastinum has become a part of the pericardial sac sealing the defect.

2. Total excision of the pericardial sac was discussed before and at the time of operation, since there was reason to believe from analysis of the available data that it could be removed safely. Not knowing the mechanism of the formation of the fluid it appeared that two untoward consequences might ensue: (a) continued recurrence of fluid and the virtual reformation of a pericardial cavity, the parietal component being formed by the mediastinum, or (b) that adhesions might form in an irregular trabeculated fashion and fluid reaccumulate in pockets which could not be drained satisfactorily by tap.

3. Removal of part of the pericardial sac with scarification of the posterior part of it and of the heart in an attempt to produce adhesions to obliterate the cavity. This was discussed and decided against for the reason already given (2b).

4. The situation could probably be approached surgically if the pericardial sac could first be made adherent to the heart. In short, if the pericardial cavity were obliterated by adhesion of the two layers, the fibrous pericardium could be stripped off later if evidence of constriction ap-

peared. The use of irritants such as permutit[10] and powdered bone dust[11] have been considered. We have been deterred from their use by the fear of adhesions giving rise to pocket formation which we could not adequately relieve by tap.

5. The use of air or lipiodol in the pericardial cavity when fluid was removed, as has been done in the treatment of tuberculous pericarditis has been considered[12, 13]. The objections to this may be the same as those already mentioned. It is possible, however, that at some time the effects of small amounts of air left in the pericardial cavity at the time of the tap, will be tested.

There are two measures which appear to be contraindicated in the treatment of pericardial effusion per se, but may, of course, be required for another condition which may be present. If these opposing interests arise, the need for these measures would have to be balanced against the contraindications. We refer to venesection and to the use of digitalis. First with regard to venesection: the rise in venous pressure in this situation is a measure of the degree of obstruction to the inflow of blood, and of the extent the cardiac output is decreased thereby (Fig. 4). This head of pressure is required to force blood into the heart because of the increased intrapericardial pressure; lowering venous pressure by venesection may bring it to the level of the intracardiac pressure, a situation in which no blood would enter the right heart. With respect to the use of digitalis, there is this to be said: Stewart and Cohn[14] have shown and Stewart and his coworkers[15, 16] have demonstrated again the observation that digitalis decreases the size of the heart. Giving digitalis presumably would make an organ whose diastolic size is already encroached on smaller still, a result which does not appear to be beneficial under these circumstances. On the other hand, with respect to its effect on contraction, namely an increase[17], it would appear to be superfluous, because the heart is in all likelihood putting out in unit time all the blood which gets into its cavities.

OBSERVATIONS

Effect of Pericardial Effusion on Cardiac Output. There was opportunity to measure the cardiac output on several occasions before and again after pericardial tap. On April 30, 1935, after 1100 c.c. (1st tap) had been removed on April 24, 1935, the cardiac output measured 3.00 liters, equivalent to 3.00 l./sq.m/min., and 26 c.c. per beat (Fig. 1). On May 24, 1935 when fluid had reaccumulated and the patient exhibited the signs and symptoms of cardiac tamponade which have been described, the cardiac output had fallen to 2.03 l./min., which amounted to 1.83 l./sq.m/min. and 20 c.c. per beat. On May 25, 1935, 600 c.c. of fluid was removed (2nd tap) and 48 hours later the cardiac output had increased to 2.46 l./min. or 2.26 l./sq.m/min. and 25 c.c. per beat. Results similar to these were obtained on three other occasions (the third tap, June 21, 1935, the seventh, November 6, 1935, the thirteenth, February 27, 1936). In short, the cardiac output per minute, and cardiac index and output per beat were decreased when fluid was present in the pericardial cavity and increased following its removal. The measurements made after the exploratory operation revealed no significant trends from those recorded before operation (Fig. 1, February 27, 1936).

Effect on Venous Pressure. The venous pressure was measured whenever the cardiac output was estimated, as well as on many other occasions. The accumulation of fluid in the pericardium was found to be associated with rise in venous pressure, varying between 159 and 235 mm. saline (Fig. 1), at the time the cardiac output was diminished, and fell to normal level after tap (55 to 83 mm. saline), the cardiac output now having increased.

Effect on Circulation Time. The arm to tongue circulation time varied between 10.6 and 11.2* seconds when pericardial effusion was present and became shorter on each occasion after tap, falling so that the range became

* The average time for normal children from 8 to 16 years of age is 8.6 seconds, the range 5.0 to 13.5 seconds (18).

6.1 to 9.8 seconds (Fig 1). The longer circulation times were found when the cardiac output was decreased and the venous pressure elevated and the shorter ones after tap when the cardiac output was greater and the venous pressure normal (Fig. 1).

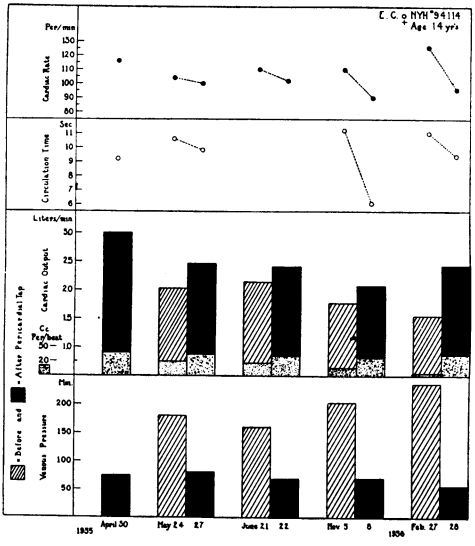
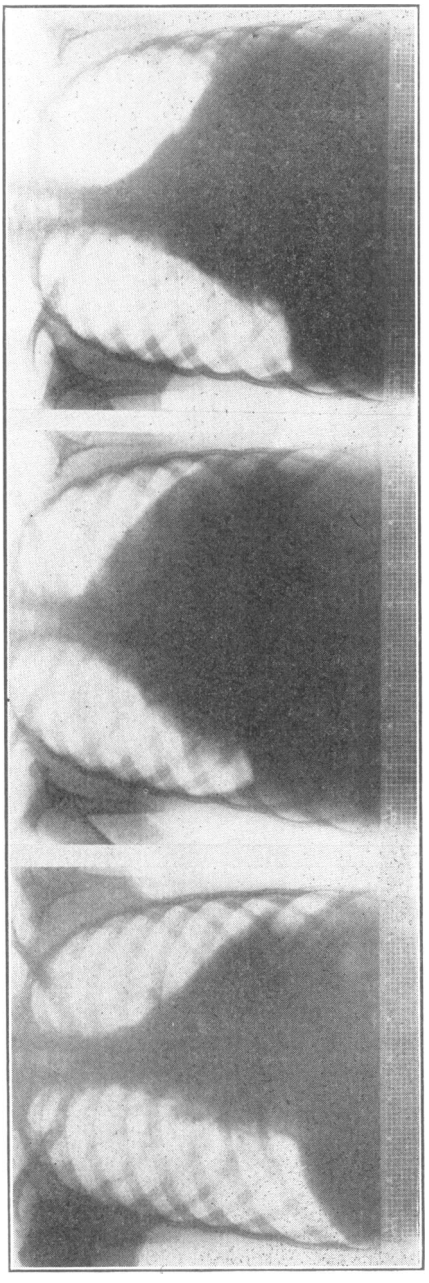


Figure 1,

In this figure are presented data relating to venous pressure, cardiac output, circulation time and cardiac rate in the presence of pericardial effusion. Observations are recorded before as well as after pericardial tap.

Effect on Cardiac Rate. The heart rate was faster when the sac was distended with fluid than it was after pericardial tap (Fig. 1). This was found to be the case on each occasion; the slowing resulting from relief of the tamponade was, however, greater on some occasions than on others. This variation is no doubt accounted for by the amount of fluid which was present before tap, and the amount removed.

Effect on Blood Pressure. The blood pressure followed no fixed pattern. It was low when the patient was in her



2a 2b 2c

Figure 2

In this figure are reproduced x-ray photographs of the cardiac silhouette taken at a distance of 2 meters. Photograph 2a was taken on April 30, 1935 after pericardial tap; 2b was taken on May 24, 1935 before, and 2c on May 25, 1935 after 600 c.c. of fluid was removed from the pericardial cavity.

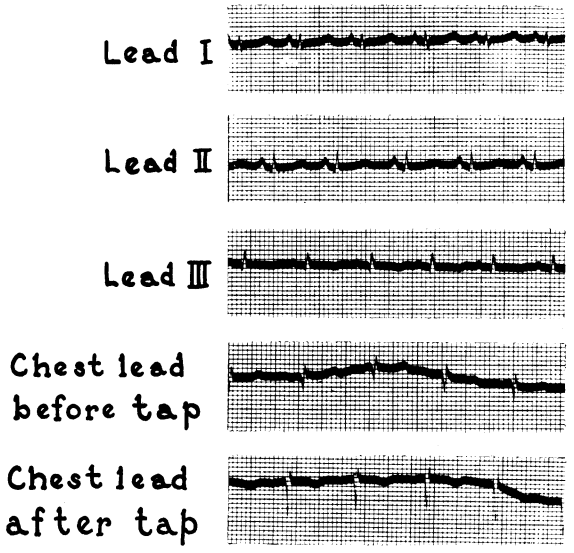


Figure 3

In this figure are shown electrocardiographic records of this patient. From above downward the first 4 photographs are Leads I, II, III and IV (chest lead) respectively, taken on May 24, 1935 when there was fluid in the pericardial cavity. The record at the bottom is lead IV (chest lead) taken on May 27, 1935 after 600 c.c. of fluid was removed from the pericardial cavity.

best state; since pericardial tap was at times followed by slight rise and at other times by slight fall in pressure no conclusions can be drawn from this case.

Effect on Cardiac Silhouette. When there was fluid in the pericardial sac the cardiac silhouette was large and became correspondingly smaller after tap, but not all of the fluid being removed the true size of the heart was not revealed. It did not appear large, however, either on physical examination or when it was exposed at operation (November 15, 1935). When there was fluid in the pericardial cavity the cardiac silhouette assumed the water bottle configuration commonly associated with this lesion (Fig. 2b., May 24, 1935). Its shadow had decreased in size (Fig. 2c.) on May 27, 1935, after the removal of 600 c.c. of

fluid. In Figure 2a, April 30, 1935, the cardiac silhouette was the smallest that has been recorded.

Electrocardiograms. The electrocardiogram showed QRS complexes of low magnitude (Fig. 3) in all leads. There was no significant change in the electrical axis with change in position of the patient, either when there was fluid in the pericardial cavity, or after its removal, or after the exploratory operation. On several occasions the amplitude of the QRS complexes in the chest lead[19] increased after pericardial tap (Fig. 3).

Effect on Vital Capacity. The vital capacity of the patient was decreased with respect to that of a normal girl of her age*. The vital capacity on all but one occasion was less when the fluid was present in the sac than after tap. One set of observations may serve as an example: The vital capacity on May 24, 1935, measured 900 c.c. After removal of 600 c.c. of pericardial fluid, the vital capacity on May 27, 1935 measured 1100 c.c. To a certain extent the alterations in vital capacity are no doubt reflections of the encroachment of the pericardial contents upon the space usually occupied by the lungs.

Effect of Pericardial Tap on Output of Urine. On the occasion of the twenty-third admission, November 16, 1936, the patient remained in bed two and a half days before tap and two and a half days after pericardial tap, in order to keep account of the fluid intake and output. The output of urine was approximately three times greater the day after tap than the day before (1020 c.c. and 385 c.c. respectively). In short, the output of urine appeared to increase following tap.

Discussion

It appears therefore that when fluid accumulated in the pericardial cavity in sufficient quantity to give tamponade effect the venous pressure rose, the cardiac output became less, the output per beat smaller, the circulation time

* According to the Wilson and Edwards (20) standards the vital capacity of this patient on May 27, 1935 was approximately 50 per cent below the average for her size.

longer and the heart rate faster. On removal of the fluid by mechanical means (tap) the venous pressure fell, the cardiac output increased per minute and per beat, the circulation time became shorter and the heart rate slower (Fig. 1). In other words, there is great decrease in the capacity of the heart as a pump when there is increase in fluid in the pericardial cavity. The fluid in the sac interferes with the filling of the heart and as it increases there is progressive increase in its interference, which is objectively identified by the rise in venous pressure. The cardiac output per minute and per beat appear to decrease because of the decrease in amount of blood that enters the right heart; for the heart can put out only the amount of blood that is available to it; moreover, since the diastolic size of the heart is restricted its output may be decreased because of limitation of extent of its contraction. A correlation appears between venous pressure and cardiac output in cardiac tamponade as illustrated by the case of this patient. The venous pressures (Fig. 4) have been arranged in decreasing order, disregarding chronological sequence, and

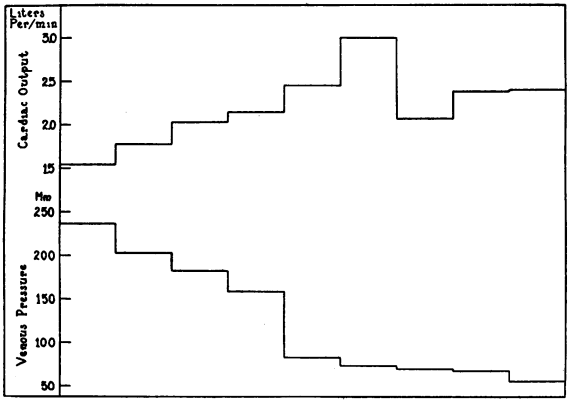


Figure 4

In this figure are recorded data relating to venous pressure and cardiac output. The observations of venous pressure have been plotted in decreasing order, disregarding chronological sequence. Above venous pressure have been plotted the corresponding measurements of cardiac output (see text).

above them have been plotted the corresponding levels of cardiac output (Fig. 4). A step-like decrease in venous pressure is associated with a step-like rise in cardiac output. For the elevated venous pressures the two curves are approximately mirror images of each other. At the higher levels of venous pressure (235 mm.) the cardiac output is greatly diminished (1.54 l./min.) and as the venous pressure falls, the cardiac output increases in a surprisingly uniform fashion, this relationship being maintained until the venous pressure has fallen to 83 mm., the normal range, where fluctuations in cardiac output are observed. This relationship attains added significance through consideration of the fact that these observations were made over a period of many months and are plotted without chronological sequence. The rise in venous pressure appears then to give a measure of the decrease in cardiac output and the degree of tamponade.

On two occasions the pressure in the pericardial sac was measured and found to be 100 mm. and 75 mm. of the fluid, respectively. The effect of removal of successive increments of fluid on the venous pressure was observed on two occasions. On inserting the needle into the pericardial cavity the venous pressure fell sharply from 198 mm. to 155 mm. on February 27th, 1936 (Fig. 5). In short, the fluid which flowed into the tapping system was sufficient to relieve tension in the sac; the venous pressure then fell rapidly with the removal of each 50 to 100 c.c., reached 100 mm. when about 400 c.c. had been removed and after that its fall was more gradual. Results indicating similar trends were observed on the second occasion. These observations do not throw light on the degree of distensibility of the pericardium in normal human beings, since in this case it underwent frequent stretching and remained distended so long that it remained large permanently and did not shrink to encase the heart completely at any time. This was the observation at operation, for after removal of the fluid it was left as a thin walled, wrinkled sac, it is this which filled until tamponade occurred. In this instance, considerable amounts accumulated before embarrassment

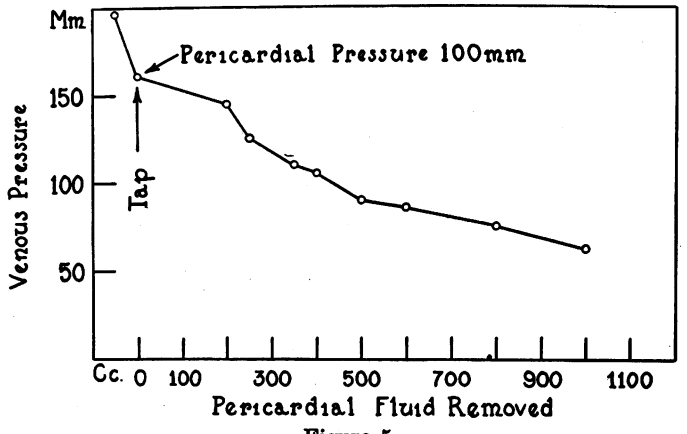


Figure 5

In this figure is shown the fall in venous pressure with the removal of successive amounts of pericardial fluid, together with the intrapericardial pressure.

was evident. Care was exercised at each tap to remove fluid slowly in order to allow for circulatory adjustments and to prevent rapid dilatation of the heart.

Fineberg[1] has found in acute pericardial distention that approximately one-third the weight of the heart in cubic centimeters of saline can be injected into the pericardial cavity before interference with ventricular filling (estimated by rise in venous pressure) occurred in dogs. He makes the estimation that 80 to 100 c.c. of pericardial fluid can be present before a rise in venous pressure occurs, if relations observed in animals obtain in human beings. As a consequence of these observations it may be inferred that the pericardial sac offers ample margin by which the normal heart may dilate. What is measured under the conditions of Fineberg's observations may not be so much the degree of distention of the pericardium but rather the amount the heart volume may be compressed or encroached upon.

The mechanism of formation and absorption of pericardial fluid is not understood. The lymphatic drainage has not been adequately studied. It was thought that the absorption of dyes from the pericardial cavity in this

patient might throw some light on the size of the molecules that could be absorbed from this cavity. The plan was as follows and observations were made on two occasions: After removal of as much pericardial fluid as possible and while the needle was still in place phenolsulphonephthalein 2 c.c. was injected into the cavity. The rate of excretion of the dye in the urine was followed. On the first occasion, January 18, 1936 (eleventh tap, 1200 c.c.) more than 75 per cent of the dye was recovered in the urine within 24 hours; one of the intermediary specimens was lost and the total amount excreted is not known. On the second occasion, September 16, 1936 (twenty-second tap, 1800 c.c.), 99 per cent of the dye was excreted in twenty-five and one-half hours. The excretion was somewhat slow in reaching a maximum but was for the most part all removed from the cavity in twenty-four hours. Thus, this dye given intrapericardially reaches the blood, and finally the kidney.

On the other hand, the dye given intravenously apparently did not find its way into the pericardial cavity. On November 19, 1936, at 1 p.m. phenolsulphonephthalein 1 c.c. was given intravenously. At 1:30 p.m. pericardial tap number 23 was performed and 1000 c.c. of fluid removed. Dye could not be detected in the pericardial fluid; the patient had excreted all the dye in the urine at the end of four hours.

On one occasion, June 2, 1936 (eighteenth tap, 650 c.c. of fluid) vital red, 1.0 c.c. of 1.5 per cent solution for each 5 kgm., a total of 6 c.c., a dye having a larger molecule than phenolsulphonephthalein was placed in the pericardial cavity at the conclusion of the tap. Colorimetric titration was not resorted to but amounts detectable by the naked eye were not excreted in the urine in the following thirty-five hours. At the time of the next tap (the nineteenth) on July 1, 1936, that is, twenty-nine days later, the fluid removed was dark pink in color (usually greenish yellow) indicating the presence of the dye at the end of one month and that it had not been absorbed. On February 2, 1936, the patient was given 3 c.c. of 1.5 per cent vital red at 1:15

p.m. intravenously. At 5:15 p.m. pericardial tap was done and 1150 c.c. of fluid was removed. The dye could not be detected in the fluid on gross examination. In short, dye of this size molecule given intravenously does not find its way into the pericardial fluid at the end of four hours. From these observations we make the inference that molecules of the order of phenolsulphonephthalein were absorbed readily from the pericardial cavity while the larger molecule represented by vital red was not absorbed but remained in the cavity. On the other hand, neither the small molecule of phenolsulphonephthalein nor the larger one of vital red, in the concentrations given, found their way out of the circulating blood into the pericardial cavity at the time of examination. In all likelihood the small molecule of phenolsulphonephthalein was removed from the pericardial fluid by way of the sub-epicardial capillaries.

Our observations with respect to the absorption of dyes of different molecular sizes no doubt find their explanation in the observations made by Drinker and Field[21] relating to absorption from the pericardial cavity in rabbits. They found that simple solutions are absorbed by the sub-epicardial blood capillaries; on the other hand, serum and graphite particles were removed very slowly. The small molecular size of phenolsulphonephthalein apparently permits of its ready transfer into the sub-epicardial capillaries; the large size of the vital red molecule no doubt places it in the category represented by serum and graphite particles. Entrance into the lymphatic stream from the pericardial cavity apparently occurs only with the greatest difficulty and very slowly (Drinker and Field[21]).

We have no data which permit us to draw conclusions regarding the nature of the defect which is responsible for the formation of pericardial fluid in excessive quantities in this patient. The chemical nature of the fluid in all probability accounts for its not being absorbed. The fluid on one occasion, April 20, 1936 (sixteenth tap) had approximately the same total protein content (both albumin and globulin) as the blood of this patient; the osmotic pressure of the two fluids would be approximately identical; this

being the case there would be no opportunity for the passage of fluid from the cavity into the sub-epicardial blood capillaries. On another occasion (the twenty-third tap on November 19, 1936) the total protein content of the pericardial fluid (seventeenth tap) measured 4.2 grams per cent (albumin 1.2 gm., globulin 2.6 gm.) and the serum protein 6.7 gm. per cent (albumin 2.9 gm., globulin 2.9 gm.).

SUMMARY

The case of a patient whose presenting lesion is recurrent chronic pericardial effusion has been described. On the basis of the negative data which have been accumulated the etiology is at present unknown. That it is the result of a chronic low grade infection must be kept in mind. The usual clinical evidences of infection are, however, lacking. That it may be a disturbance in the mechanism of formation or resorption of pericardial fluid is a possible explanation. Evidence in favor of this may be found in the observation that the mesothelial layer of cells lining the parietal pericardium were lacking. Whether this layer of cells was stripped off during its removal, fixing and preparation for examination we are unable to state. The very nature of the fluid found in this particular case, in the light of known facts, makes its resorption difficult once it has been poured into the cavity. Exploratory operation after one year has not appeared to alter the course of the disease significantly. The possibility of further surgical intervention has been discussed without having the way made clear as to the best procedure.

We have had occasion to make many clinical observations in this patient and these allow us to restate the clinical manifestations of cardiac tamponade which develop gradually: (1) The evidence of obstruction to entrance of blood into the heart is revealed by the distended veins, particularly those of the neck, and objectively by a rise in venous pressure; (2) dyspnea; (3) edema of the face, eyelids and forehead; (4) pulmonary congestion and pleural effusion; (5) enlargement of the liver; (6) ascites; (7) edema of the extremities; (8) tachycardia; (9) paradoxical pulse has

been a constant finding in our experience; (10) the heart sounds may be distant; (11) the area of cardiac dullness is increased and Ewart's sign, and Rotch's sign may be found; (12) the Roentgen ray photograph reveals the water-jug contour and on fluoroscope examination, the diminution or absence of cardiac pulsation may be observed; (13) in our experience there has been no correlation of blood pressure changes with the presence of fluid; the pulse pressure is usually small; (14) the electrocardiograms obtained of this patient as well as those already recorded in the literature, indicate that the QRS complexes are usually of low voltage in the presence of pericardial effusion. This configuration of the electrocardiogram does not appear to be pathognomonic of pericardial effusion, for, to give one illustration, it appears to be characteristic also of chronic constrictive pericarditis.

Our studies of the circulation have revealed these facts: In the presence of chronic pericardial effusion in the case of this patient (1) there occurs a rise in the venous pressure; (2) the circulation time becomes longer; (3) the cardiac output per minute and, more significantly, per beat is diminished; (4) the intrapericardial pressure is increased; (5) the rise in venous pressure appears to be a very good measure of limitation in cardiac output in this instance, for it seems to be a fact that successive increments of rise in venous pressure result in decrease in cardiac output. There is change in the reverse direction of all these with removal of pericardial fluid.

We have made certain observations on the passage of dyes from the pericardial cavity into the circulation and from the circulation into the pericardial cavity. We chose two dyes; one, phenosulphonephthalein, has a small molecule. It appears that it finds its way with moderate rapidity from the pericardial cavity into the blood stream and is excreted in the urine in its total amount in approximately twenty-four hours. On the other hand, vital red, having a larger molecule, introduced into the pericardial cavity was present in its fluid four weeks later, and detect-

able amounts did not appear in the urine. It is likely that the removal of the small molecule of phenolsulphonephthalein was by way of the sub-epicardial capillaries as Drinker and Field[21] have found to be the case in rabbits.

These same dyes introduced intravenously did not appear in the pericardial fluid at the times observations were made. The similarity in the protein content of the blood may account for failure of resorption of the fluid.

From our clinical and laboratory examinations as time has gone on, no developments have appeared which lead us to a clearer understanding of this puzzling case.

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